NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NEWSLETTER

MARCH 2024 | VOLUME 3 | ISSUE 3

FASTEST

FVIIa for Acute hemorrhagic Stroke

Administered at Earliest Time

Issue Contents:

Message from Dr. Demchuk

We are honored to be featured in this month's FASTEST trial newsletter. It has been a real team effort to beat the clock! The entire team is really enthusiastic about the trial question. We have embraced the challenge of trying to enroll patients within the golden first 2 hours of ICH. We view this as opportunity for us all to be part of history repeating perhaps. Our efforts to establish a medical therapy in ICH in an ultra-early time window is very similar to what the NINDS tPA trial accomplished in ischemic stroke (enrolling half under 90 minutes). Our pre-notification system, STAT stroke parallel workflow, stroke fellow assessment at triage, coordinator on call and deferral of consent process have all created time efficiencies for us to achieve a median door to study drug time of ~40 minutes.

Andrew Demchuk MD, FRCPC
Professor of Neurology
Director of Calgary Stroke Program,
Departments of Clinical Neurosciences & Radiology

Please join us for the *FASTEST* Monthly Webinar

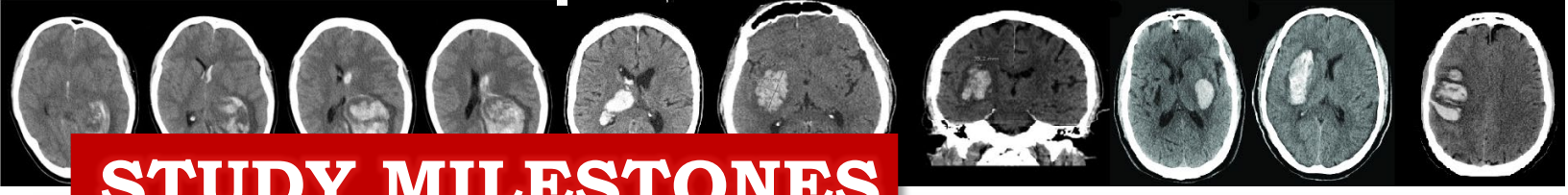
Wednesday March 20th, 2:00-3:00 pm EST

- Dr. Atif Zafar and his team from St. Michael's Hospital, Toronto will be discussing case at their site.
- Trial Status update and interim analysis results.
- Dr. Broderick will be discussing AE, SAE and Adverse Events of Special Interest (AESI) reporting in detail.
- Pharmacy IP update.
- NDMC will be discussing F246 and the new StrokeNet WebDCU User Manual.
- Managing IP Temperature Monitoring.

Join Zoom Meeting

https://ucincinnati.zoom.us/j/94084789726

Prior presentations and slides are available at, https://www.nihstrokenet.org/fastest/webinars



STUDY MILESTONES

Total Sites Released to Enroll: **78** (**44** USA, **34** OUS: **6** Germany, **14** Japan, **4** Spain, **6** Canadian, **4** UK)

Total MSUs Released to Enroll: **12** (**10** US and **2** OUS)

Total Randomization = **407**

- US Randomizations: **116**
- International randomizations: **291**
  - Japan = **191**
  - Canada = **49**
  - Spain =**25**
  - Germany = **18**
  - UK = **8**

Randomization last month = **31**

Total Screen Failures = **1423**

Subjects Randomized by MSU = **16**

Subjects Terminated Early = **2**

eConsent Used = **16**

Remote Consent Used = **12**

CALENDAR OF EVENTS

Upcoming *FASTEST* Monthly Webinars: **Wednesday, Mar 20th, @ 2:00-3:00 pm EST**

FASTEST study team office hours: **Monday, March 25th, @ 1:00-2:00 pm.**

FASTEST ENROLLMENTS

Kobe City Medical Center General Hospital in Kobe, Japan, has been awarded the FASTEST Enrollment Trophy for 2023!

Overall Top Enrolling Sites			
Country	**Site ID**	**Site Name**	**Total Subjects Randomized**
Canada	1539	University of Calgary - Foothills Medical Centre, Calgary, AB, Canada	22
Germany	2230	Tubingen University Hospital, Tubingen, Germany	7
Japan	1961	National Cerebral and Cardiovascular Center, Osaka, Japan	45
Spain	1670	Vall d'Hebron Hospital, Barcelona, B, Spain	9
UK	2560	Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom	4
US	1123	Memorial Hermann Texas Medical Center, Houston, TX	21
Top Enrolling Sites for 2023			
Country	**Site ID**	**Site Name**	**Total Subjects Randomized**
Canada	1539	University of Calgary - Foothills Medical Centre, Calgary, AB, Canada	12
Germany	2233	Clinic Frankfurt Hoechst, Frankfurt, Germany	3
Japan	1967	**Kobe City Medical Center General Hospital, Kobe, Japan**	32
Spain	1663	Girona University Hospital, Girona, GI, Spain	5
UK	2560	Royal Victoria Infirmary, Newcastle upon Tyne, United Kingdom	4
US	1123	Memorial Hermann Texas Medical Center, Houston, TX	9

New Sites…Welcome Aboard!

The following new sites were **released to enroll** in the *FASTEST* study during the last month.

Kaiser Permanente Riverside Medical Center, Riverside, CA

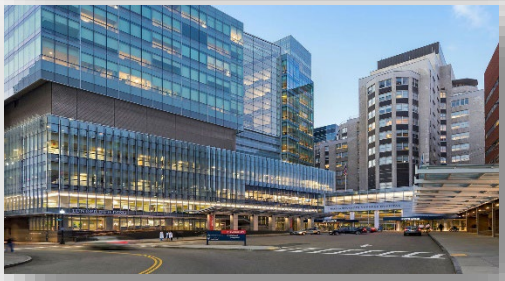
Site PI:
Navdeep S Sangha, MD

San Francisco General Hospital, San Francisco, CA

Site PI:
Vineeta Singh, MD

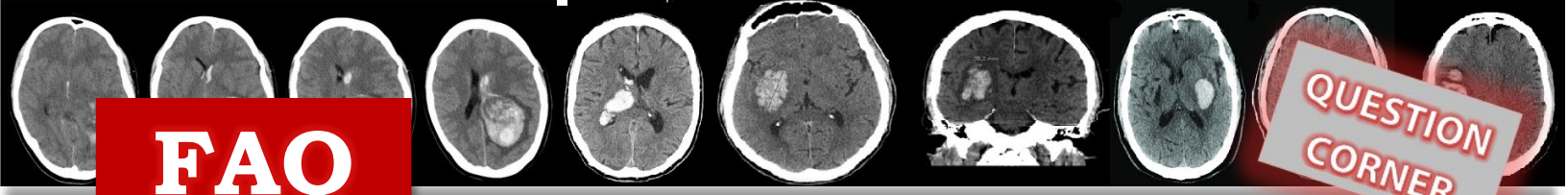
Congratulations on 1st Enrollment!!!

Congratulations to Dr. Anna KHANNA and her team at the UF Health Shands Hospital, Gainesville, FL for enrolling their first subject in FASTEST.



Congratulations to Dr. Pierre BORCZUK and his team at the Massachusetts General Hospital, Boston, MA for enrolling their first subject in FASTEST.

Congratulations to Dr. Christopher LEWANDOWSKI and his team at the Henry Ford Hospital, Detroit, MI for enrolling their first subject in FASTEST.



Q: We want to add the MSU manager to the DoA but I am not certain what role would be appropriate. She completed the CITI HSP but not the GCP as it is not a requirement for research in CDH. For her to be added as a sub-Investigator, she would need to complete the GCP training?
A: It really depends on what the investigator's role in the study will be. Will MSU manager be doing trial specific assessments or procedures? If so, then yes, she would need to be on the DoA and complete all the training required per her role and responsibilities. If she will be practicing standard of care duties NOT specific to the trial, then she would not be required to be on the DoA.

Q: A subject was transitioned to comfort care at our site. What are the appropriate steps?
A: If a subject is transitioned to comfort or palliative care post-enrollment, and the family opts not to continue subject follow-up, this would constitute the End of Study (EOS) for the subject. However, if the family consents to ongoing follow-up, please ensure to meticulously document the date and time of the patient's passing, as this will serve as the EOS date. It's important to note that regardless of the scenario, no further laboratory tests or assessments need to be conducted once the patient has been transitioned to comfort, palliative, or hospice care at the family's request. Kindly follow the instructions/note on page 43 of the Study MOP Version 2 for details.

Q: Is Intraosseous administration is permitted for FASTEST?
A: Per FASTEST study protocol, Intraosseous administration is **not permitted**.

Q: Could you please assist me in understanding this statement and clarify whether our facility is required to initiate stroke screenings for patients already in the hospital when a "Code Stroke" is announced during their stay?
A: Yes, we are also enrolling subjects who have been admitted to the hospital and experience a stroke during their hospital stay. As mentioned in the data collection guidelines, your facility is expected to conduct stroke screenings for patients already in the hospital when a "Code Stroke" is announced. In the specific case you described, the patient should have been considered for enrollment in the FASTEST study if she met all the inclusion and exclusion criteria after screening. If the patient did not meet the criteria outlined in the inclusion and exclusion guidelines and was therefore not eligible for enrollment, they should have been documented in the screen failure log.

Q: In terms of females of child-bearing potential, is it mandatory to order the pregnancy test upon hospital admission as part of the enrollment eligibility process? or if the pregnancy test gets ordered on EPIC by the ED attending, does it need to be resulted to exclude pregnancy prior to administration of drug?
A: While the pregnancy test is recommended, it is not mandatory**.** However, it would be beneficial to conduct the test for women of childbearing age who do not have a legally authorized representative (LAR) accompanying them or do not have a confirmed pregnancy status. Notably, it is not a requirement prior to randomization because the drug **does not cross the placental barrier**, and there are no known adverse effects on the fetus.

Q: To our knowledge at the time of enrolment, the patient was not pregnant and gave birth last year. Unfortunately, we did not realize she was still lactating until after the fact. Also, her bedside exam (which included some mixed aphasia) was a bit limiting and husband did not provide additional details. Is this eligibility violation according to the exclusion criteria #22?
A: The lactation criterion is intended to identify women who have recently given birth and are at risk of venous thrombosis. Women who are lactating **beyond the 12-week postpartum period are not excluded from participation.** However, women who are breastfeeding at the time of enrollment should refrain from breastfeeding for 24 hours after drug administration, considering the study drug's half-life of 2-3 hours.

Q: Who can compound the study drug?
A: Trained Pharmacy staff, physicians (PI AND Sub-I) and RNs or trained Coordinators with a **medical license** including drug compounding within their scope of practice can compound and prepare study drug for administration. There is no need to delegate this responsibility on the DoA and should be a study team determination. Training on compounding study drug video can be found in the WebDCU training campus under the FASTEST project WebDCU™ Campus - Training Center (musc.edu).

Please send in your questions and we will address them accordingly and share with others in the next Newsletter.

SHOUT OUTS!!

Congratulations to US sites that have completed EFIC and have been approved for emergency consent

1. **Washington University Barnes Jewish, St. Louis MI**

Thank you to the sites recently released to enroll for their hard work:

1. **San Francisco General Hospital, San Francisco, CA**
2. **Kaiser Permanente Riverside Medical Center, Riverside, CA**

The Top Enrolling Site

Congratulations to **National Cerebral and Cardiovascular Center, Osaka, Japan** for being the highest enrolling site in the study.

Subjects enrolled = 46!!

Congratulations to Enrolling Sites last Month!

Kyorin University Hospital, Tokyo, Japan	1 Subject
National Cerebral and Cardiovascular Center, Osaka, Japan	6 Subject
Niigata City General Hospital, Niigata, Japan	2 Subject
Iwate Prefectural Central Hospital, Morioka, Japan	3 Subject
NHO Osaka National Hospital, Osaka, Japan	1 Subject
Ottawa Hospital, Ottawa, ON, Canada	1 Subject
St. Michaels Hospital, Toronto, ON, Canada	1 Subject
Girona University Hospital, Girona, GI, Spain	2 Subject
Santa Creu and Sant Pau Hospital, Barcelona, B, Spain	1 Subject
UF Health Shands Hospital, Gainesville, FL	1 Subject
Memorial Hermann Texas Medical Center, Houston, TX	2 Subject
The Queen's Medical Center, Honolulu, HI	1 Subject
Henry Ford Hospital, Detroit, MI	1 Subject
Grady Memorial Hospital, Atlanta, GA	2 Subject
Mills Peninsula Medical Center, Burlingame, CA	1 Subject
M Health Fairview Ridges Hospital, Burnsville, MN	1 Subject
M Health Fairview Southdale Hospital, Edina, MN	1 Subject
Charite University Medicine Berlin, Berlin, Germany	1 Subject
Tubingen University Hospital, Tubingen, Germany	1 Subject

SCIENCE CORNER

ARTICLE OF THE MONTH

Long-Term Risk of Arterial Thrombosis After Intracerebral Hemorrhage: MUCH-Italy

Alessandro Pezzini, Licia Iacoviello, Augusto Di Castelnuovo, Simona Costanzo, Barbara Tarantino, Giovanni de Gaetano, Marialuisa Zedde, Simona Marcheselli, Giorgio Silvestrelli, Alfonso Ciccone, Maria Luisa DeLodovici, Lucia Princiotta Cariddi, Maurizio Paciaroni, Cristiano Azzini, Marina Padroni, Massimo Gamba, Mauro Magoni, Massimo Del Sette, Rossana Tassi, Ivo Giuseppe De Franco, Anna Cavallini, and on behalf of the MUCH-Italy Investigators

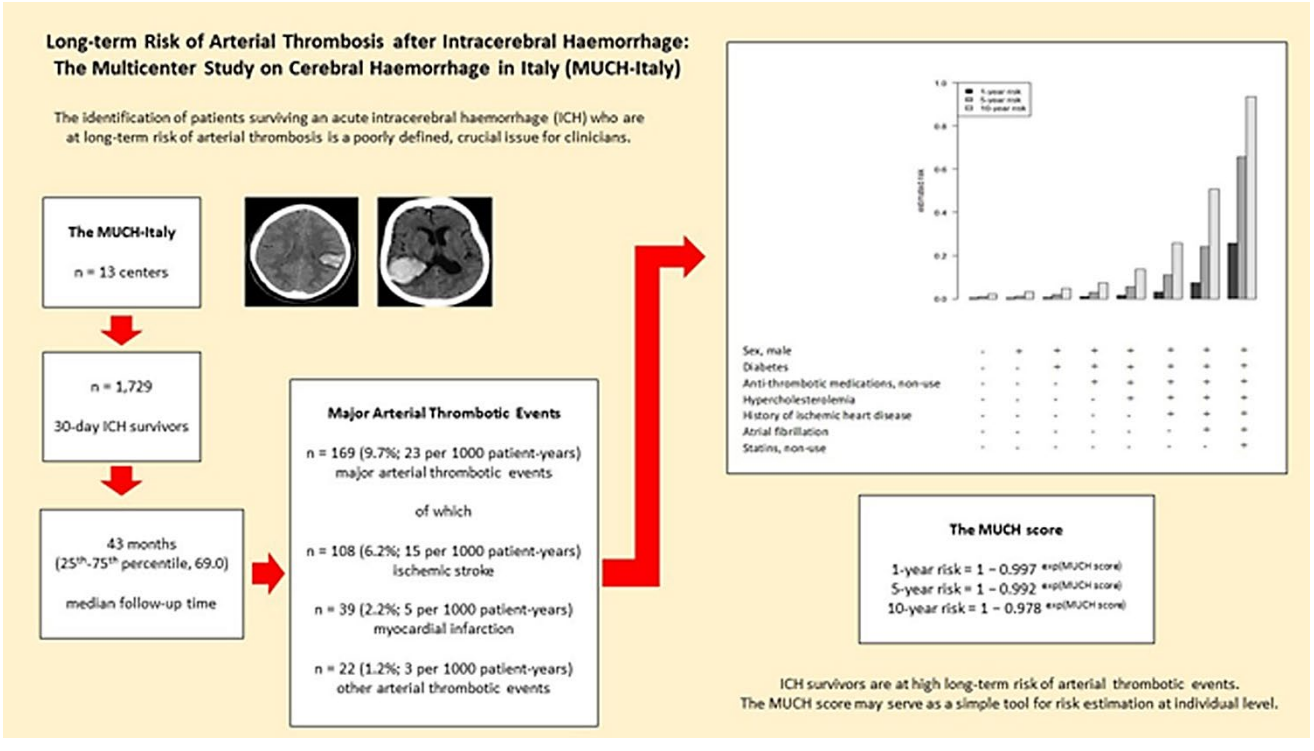
Originally published1 Feb 2024https://doi.org/10.1161/STROKEAHA.123.044626Stroke. 2024;55:634–642

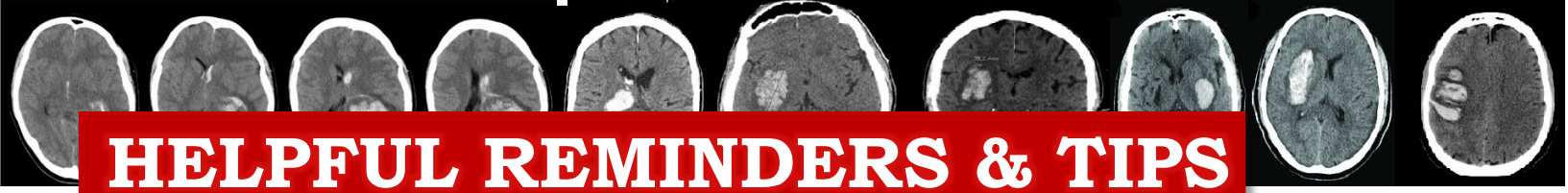
Background: The identification of patients surviving an acute intracerebral hemorrhage who are at a long-term risk of arterial thrombosis is a poorly defined, crucial issue for clinicians.

Methods: In the setting of the MUCH-Italy (Multicenter Study on Cerebral Haemorrhage in Italy) prospective observational cohort, we enrolled and followed up consecutive 30-day intracerebral hemorrhage survivors to assess the long-term incidence of arterial thrombotic events, to assess the impact of clinical and radiological variables on the risk of these events, and to develop a tool for estimating such a risk at the individual level. Primary end point was a composite of ischemic stroke, myocardial infarction, or other arterial thrombotic events. A point-scoring system was generated by the β-coefficients of the variables independently associated with the long-term risk of arterial thrombosis, and the predictive MUCH score was calculated as the sum of the weighted scores.

Results: Overall, 1729 patients (median follow-up time, 43 months [25th to 75th percentile, 69.0]) qualified for inclusion. Arterial thrombotic events occurred in 169 (9.7%) patients. Male sex, diabetes, hypercholesterolemia, atrial fibrillation, and personal history of coronary artery disease were associated with increased long-term risk of arterial thrombosis, whereas the use of statins and antithrombotic medications after the acute intracerebral hemorrhage was associated with a reduced risk. The area under the receiver operating characteristic curve of the MUCH score predictive validity was 0.716 (95% CI, 0.56–0.81) for the 0- to 1-year score, 0.672 (95% CI, 0.58–0.73) for the 0- to 5-year score, and 0.744 (95% CI, 0.65–0.81) for the 0- to 10-year score. C statistic for the prediction of events that occur from 0 to 10 years was 0.69 (95% CI, 0.64–0.74).

Interpretation: Intracerebral hemorrhage survivors are at high long-term risk of arterial thrombosis. The MUCH score may serve as a simple tool for risk estimation.





HELPFUL REMINDERS & TIPS

For Project Managers, Study Coordinators & Study Teams

- A new version of the **StrokeNet WebDCU User Manual** has been added to Project Documents within the Toolbox in WebDCU.

- **Imaging Reminders:** Submit all head imaging performed as SOC within 30 hours from stroke onset to IMC (i.e., NCCT, CTA, MRI if performed)
  - Baseline/first scan obtained either in ED or MSU to determine trial eligibility AND prior to study product administration.
  - 24 (+/6) hours from stroke onset follow-up scan
  - "Unscheduled" scan obtained for clinical deterioration or immediately prior to any surgical intervention (i.e., surgical removal of ICH or IVC placement) if planned prior to 24-hour scan.
    ***Failure to obtain a pre-op scan results in missing imaging endpoint (i.e., ability to calculate ICH growth between baseline scan and unscheduled pre-op scan)

  Imaging must be submitted within 5-7 business days of subject randomization via the Ambra Health® platform.

  - Also includes submission of WebDCU F502 which is needed to process scans.

  ***Confirmation of receipt of ALL imaging is one of the requirements in triggering "Baseline through 24 hr. Payment" to your site.

From the *FASTEST* Central Pharmacy Team

- **Recent temperature excursions in IDS Pharmacy:** There have been recent reports of temperature excursions at certain sites related to the storage of the study drug within the pharmacy. We strongly encourage all site PSCs to proactively engage with their trial pharmacist. Regular communication and periodic checks with the pharmacist will help ensure the consistent monitoring of temperature conditions and mitigate the risk of excursions.
  - The TERF needs to be submitted to the NCC project manager and Strokenet central pharmacy as soon as possible.
  - The site pharmacists should remove the effected study drug by filling out the WebDCU form in a timely manner in order to trigger a resupply. The sites are advised to add more people to the DOA in order to expedite the process of documenting things in WebDCU if necessary.

- Instructions to fill out TERF from are in the toolbox in WebDCU.

- Kit #, DUN# and the Lot number could all be found in the '**Site Drug Kit Removing'** section in the WebDCU.

- Please make sure to disseminate this newsletter to you site pharmacist/s too as it may contain helpful information regarding drug compounding, storage, accountability, etc.

INTERNATIONAL SITE OF THE MONTH

Hospital Universitari Germans Trias i Pujol, Barcelona, Spain

Site PI:
Alejandro BUSTAMANTE RANGEL

Hospital Universitari Germans Trias i Pujol, located in Barcelona, Spain, is a renowned medical institution known for its commitment to excellence in healthcare, research, and education. With a rich history spanning decades, the hospital is dedicated to providing high-quality medical services to patients from Barcelona and beyond.

Germans Trias i Pujol University Hospital is named in honor of two pioneering surgeons, Joaquim and Antoni Trias i Pujol, both born in Badalona at the end of the 19th century. These distinguished individuals, natives of Badalona, rose to prominence as innovative surgeons and dedicated university professors committed to enhancing medical education. Joaquim and Antoni Trias i Pujol were born in 1888 and 1891, respectively. Their era marked the emergence of modern surgery, influenced by advancements such as anesthesia and the revolutionary ideas of Lister regarding antisepsis and later asepsis. Notably, this period saw the introduction of surgical practices in Spain by Salvador Cardenal and Miquel Fargas, who bravely performed the country's first laparotomies.

As a university hospital, it serves as a hub for medical innovation and collaboration, attracting top medical professionals and researchers from around the world. The hospital's multidisciplinary approach and state-of-the-art facilities ensure that patients receive comprehensive and personalized care across a wide range of medical specialties. Additionally, its strong focus on education and training makes it a leading institution in medical education, producing the next generation of healthcare professionals who will continue to shape the future of medicine.

STUDY CONTACTS & USEFUL INFO

For any study related queries or help please reach out to ***FASTEST*** Project managers

International Sites: **Syed Quadri** (quadrisd@ucmail.uc.edu)

United States Sites: **Emily Stinson** (stinsoey@ucmail.uc.edu)

FASTEST Clinical Hotline: 1-855-429-7050

For more information regarding the ***FASTEST*** study please visit : https://www.nihstrokenet.org/fastest/home

For prior ***FASTEST*** Presentations and Webinars slides and recordings visit: https://www.nihstrokenet.org/fastest/webinars